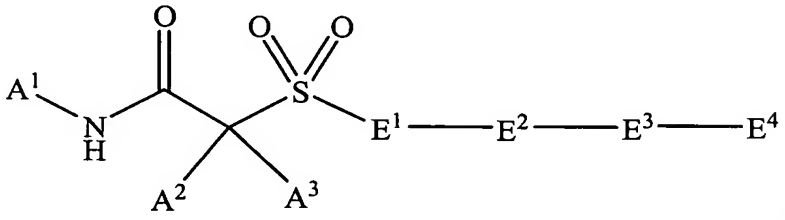
WE CLAIM:

1. A compound or a salt thereof, wherein:

the compound corresponds in structure to Formula 1-1:



(1-1); and

A^1 is selected from the group consisting of hydrogen, hydroxyl, carbocyclyloxy, and heterocyclyloxy; and

as to A^2 and A^3:

A^2 and A^3, together with the carbon to which they are both bonded, form heterocyclyl or carbocyclyl, wherein:

the heterocyclyl or carbocyclyl optionally is substituted with up to 3 independently selected R^x substituents, and

the heterocyclyl or carbocyclyl optionally is substituted with two substituents such that the two substituents, together with the atom(s) to which they are bonded, form a carbocyclyl or heterocyclyl, wherein:

the optional heterocyclyl or carbocyclyl is, in turn, optionally substituted with up to 3 independently selected R^x substituents, or

A^2 and A^3 are independently selected from the group consisting of hydrogen, alkoxyalkyl, alkylthioalkyl, alkenyl, alkynyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkenyl, carbocyclylalkynyl, carbocyclyloxyalkyl, carbocyclylalkoxyalkyl, carbocyclylalkylthio, carbocyclylthioalkyl, carbocyclylalkylthioalkyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, heterocyclyloxyalkyl, heterocyclylalkoxyalkyl, heterocyclylalkylthio, heterocyclylthioalkyl, and heterocyclylalkylthioalkyl, wherein:

any member of such group optionally is substituted with up to 3 independently selected R^x substituents, and

any member of such group optionally is substituted with two substituents such that the two substituents, together with the atom(s) to which they are bonded, form a carbocyclyl or heterocyclyl, wherein:

the heterocyclyl and carbocyclyl optionally are substituted with up to 3 independently selected R^x substituents; and

E^1 is heteroaryl, wherein the heteroaryl optionally is substituted with one or more independently selected R^x substituents; and

E^2 is carbocyclyl, wherein the carbocyclyl optionally is substituted with one or more independently selected R^x substituents; and

E^3 is selected from the group consisting of -O-, -C(O)-, -C(O)-O-, -O-C(O)-, $-N(R^b)-$, $-C(O)-N(R^b)-$, $-N(R^b)-C(O)-$, $-C(O)-N(R^b)-N(R^b)-C(O)-$, $-N(R^b)-C(O)-N(R^b)-$, -S-, -S(O)-, $-S(O)_2-$, $-N(R^b)-S(O)_2-$, $-S(O)_2-N(R^b)-$, $-O-S(O)_2-$, $-S(O)_2-O-$, -C(NH)-, -C(NOH)-, $-N(R^b)-C(NH)-$, $-N(R^b)-C(NOH)-$, $-C(NH)-N(R^b)-$, $-C(NOH)-N(R^b)-$, alkyl, alkenyl, carbonylalkyl, alkylcarbonyl, and a bond, wherein:

any alkyl or alkenyl portion of a substituent in such group optionally is substituted with one or more independently selected R^c substituents; and

E^4 is selected from the group consisting of hydrogen, halogen, cyano, alkyl, alkenyl, alkynyl, alkoxyalkyl, alkoxyalkoxyalkyl, alkylthioalkyl, alkylthioalkylthioalkyl, alkylthioalkoxyalkyl, alkoxyalkylthioalkyl, aminoalkyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkoxyalkyl, heterocyclyl, heterocyclylalkyl, and heterocyclylalkoxyalkyl, wherein:

any member of such group optionally is substituted with one or more independently selected R^d substituents; and

each R^x is independently selected from the group consisting of halogen, cyano, hydroxy, nitro, nitroso, oxo, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkoxy, R^b-oxyalkyl, alkenyloxy, alkynyloxy, alkylthio, R^bR^b-amino, R^bR^b-aminoalkyl, R^bR^b-aminoalkoxy, R^bR^b-aminoalkyl(R^b)amino, carbocyclyl, carbocyclylalkyl, carbocyclyloxy, carbocyclyloxyalkoxy, carbocyclylthio, heterocyclyl,

heterocyclylalkyl, heterocyclyloxy, heterocyclyloxyalkoxy, heterocyclylthio, alkyliminocarbonyl, alkylthioalkyl, alkylsulfonylalkyl, alkylsulfoxidoalkyl, alkylthioalkenyl, alkylsulfoxidoalkenyl, alkylsulfonylalkenyl, carbocyclylalkoxyalkyl, carbocyclyliminocarbonyl, carbocyclylthioalkyl, carbocyclylsulfoxidoalkyl, carbocyclylsulfonylalkyl, carbocyclylthioalkenyl, carbocyclylsulfoxidoalkenyl, carbocyclylsulfonylalkenyl, heterocyclylalkoxyalkyl, heterocyclylthioalkyl, heterocyclylsulfoxidoalkyl, heterocyclylsulfonylalkyl, heterocyclylthioalkenyl, heterocyclylsulfoxidoalkenyl, heterocyclylsulfonylalkenyl, heterocyclyliminocarbonyl, aminosulfonylalkyl, and $-R^{x1}-R^{x2}$, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, amino, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, and alkyl; and

each R^{x1} is selected from the group consisting of -C(O)-, -C(S)-, $-C(NR^y)-$, -S(O)-, and $-S(O)_2-$; and

each R^y is selected from the group consisting of hydrogen and hydroxy; and

each R^{x2} is selected from the group consisting of hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, alkoxyalkoxy, R^b-oxyalkyl, alkenyloxy, alkynyloxy, R^bR^b-amino, R^bR^b-aminoalkyl, R^bR^b-aminoalkoxy, R^bR^b-aminoalkyl(R^b)amino, carbocyclyl, carbocyclylalkyl, carbocyclyloxy, carbocyclyloxyalkoxy, heterocyclyl, heterocyclylalkyl, heterocyclyloxy, and heterocyclyloxyalkoxy, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen and hydroxy; and

each R^b is independently selected from the group consisting of hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, bisalkoxyalkyl, alkylthioalkyl, alkylthioalkenyl, alkylsulfoxidoalkyl, alkylsulfonyl, alkylsulfonylalkyl, carbocyclyl, carbocyclylalkyl, carbocyclyloxyalkyl, carbocyclylalkoxyalkyl, carbocyclylthioalkyl, carbocyclylthioalkenyl, carbocyclylsulfoxidoalkyl, carbocyclylsulfonyl, carbocyclylsulfonylalkyl, heterocyclyl, heterocyclylalkyl, heterocyclyloxyalkyl, heterocyclylalkoxyalkyl, heterocyclylthioalkyl, heterocyclylsulfoxidoalkyl, heterocyclylsulfonyl, heterocyclylsulfonylalkyl, aminoalkyl, aminosulfonyl, aminoalkylsulfonyl, and alkoxyalkylaminoalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkylcarbonyl, carbocyclyl, and carbocyclylalkyl; and

each R^c is independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, -C(H)(NH), -C(H)(NOH), thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, amino, alkyl, alkoxy, alkenyl, alkynyl, alkoxyalkyl, mono-alkylamino, di-alkylamino, alkylthio, carbocyclyl, carbocyclylalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, amino, alkyl, and carbocyclylalkyl; and

each R^d is independently selected from the group consisting of halogen, hydroxy, cyano, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, $-N(R^e)_2$, $-C(O)(R^f)$, $-S-R^e$, $-S(O)_2-R^e$, carbocyclyl, alkylcarbocyclyl, alkoxycarbocyclyl, carbocyclylalkyl, heterocyclyl, alkylheterocyclyl, alkoxyheterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen,

hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

each R^e is independently selected from the group consisting of hydrogen alkyl, carbocyclyl, carbocyclylalkyl, heterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

each R^f is independently selected from the group consisting of hydrogen, alkyl, $-O-R^e$, $-N(R^e)_2$, carbocyclylalkyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino.

2. A compound or salt thereof according to claim 1, wherein A^1 is tetrahydropyranyloxy.

3. A compound or salt thereof according to claim 1, wherein A^1 is hydrogen.

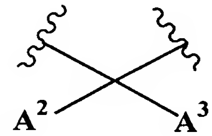
4. A compound or salt thereof according to claim 1, wherein A^1 is hydroxy.

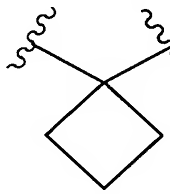
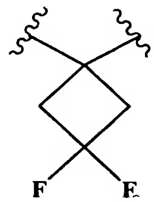
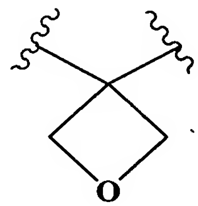
5. A compound or salt thereof according to claim 4, wherein A^2 and A^3, together with the carbon to which they are both bonded, form heterocyclyl or carbocyclyl, wherein:

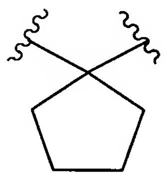
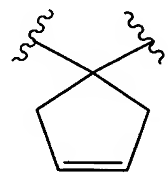
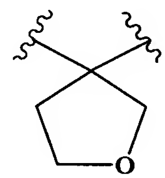
the heterocyclyl or carbocyclyl optionally is substituted with up to 3 independently selected R^x substituents, and

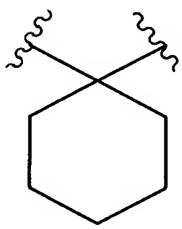
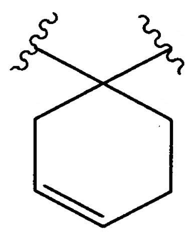
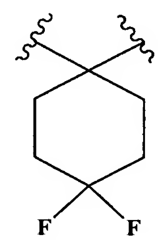
the heterocyclyl or carbocyclyl optionally is substituted with two substituents such that the two substituents, together with the atom(s) to which they are bonded, form a carbocyclyl or heterocyclyl, wherein:

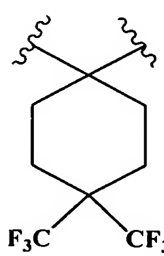
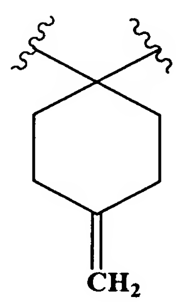
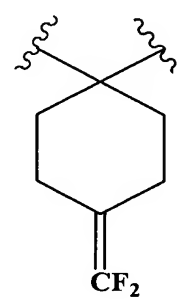
the optional heterocyclyl or carbocyclyl is, in turn, optionally substituted with up to 3 independently selected R^X substituents.

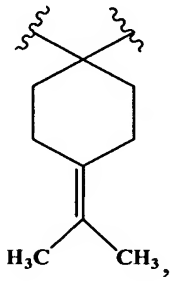
6. A compound or salt thereof according to claim 5, wherein  is selected from the group consisting of:

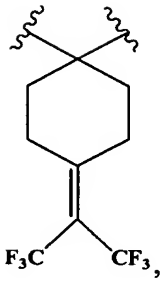
 ,  ,  ,

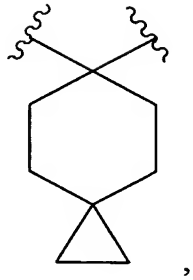
 ,  ,  ,

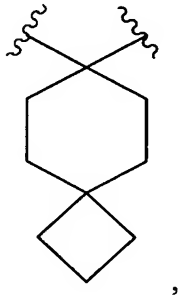
 ,  ,  ,

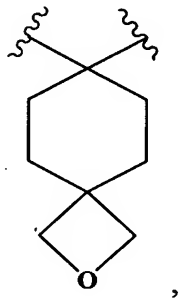
 ,  ,  ,


H3C
CH3


F3C
CF3



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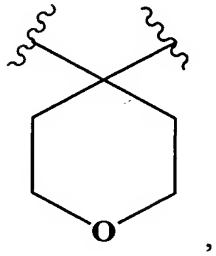
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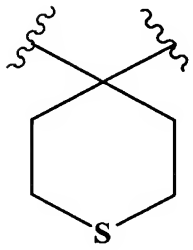
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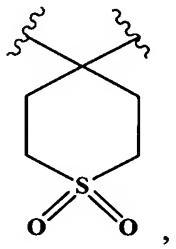
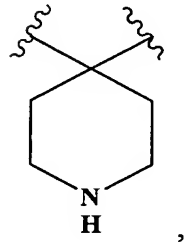
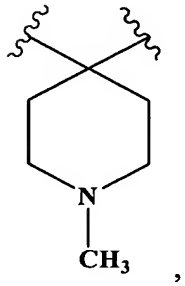

S
O
O


N
H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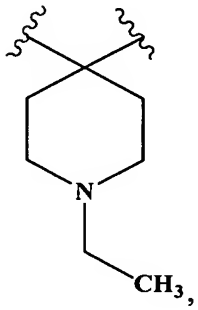
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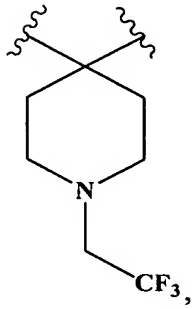
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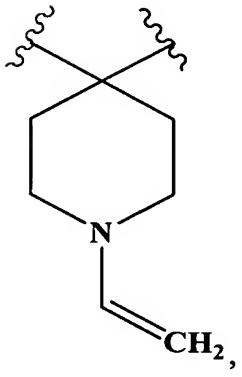
CF3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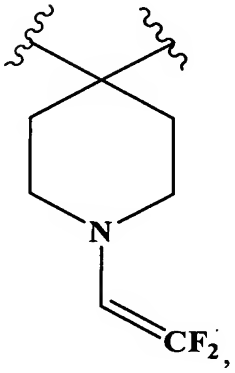
CH2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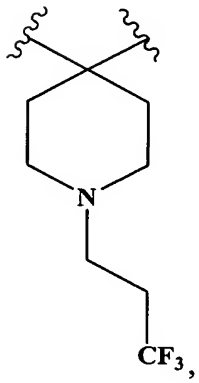
CF2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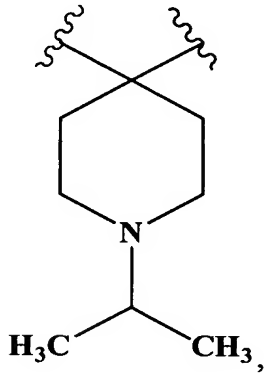
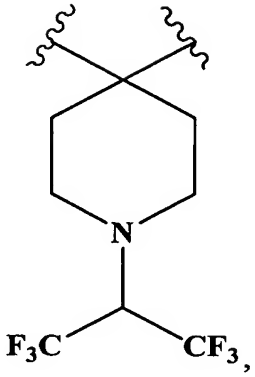
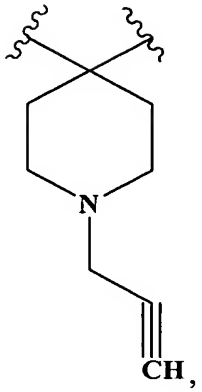
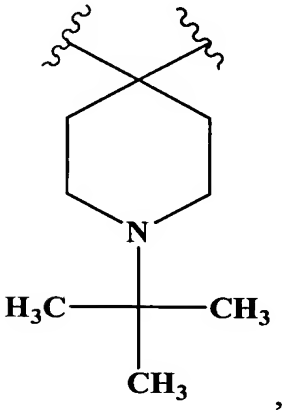
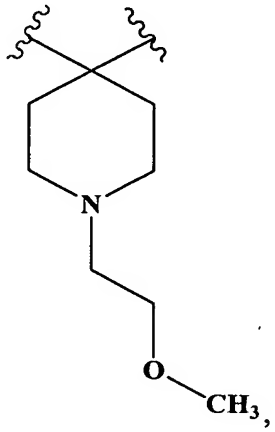
CF3

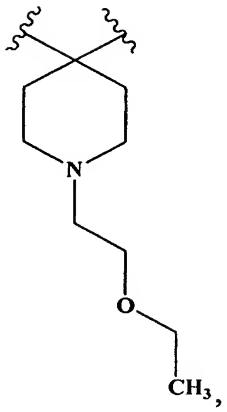


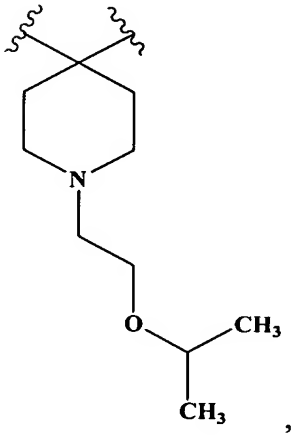


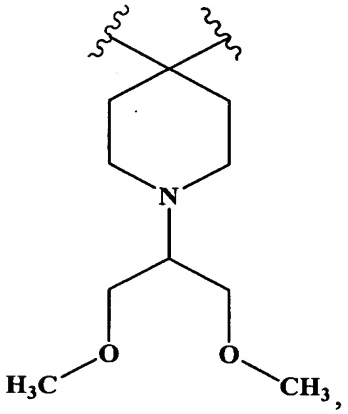


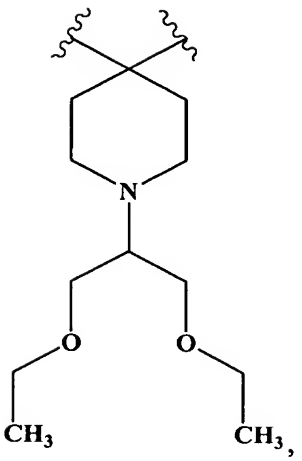


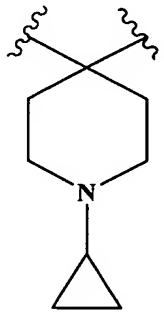








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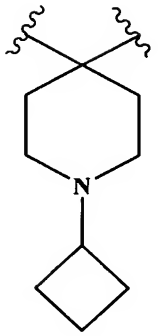
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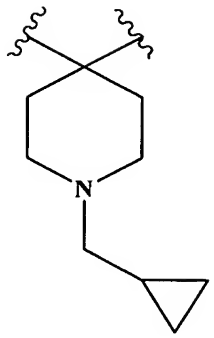
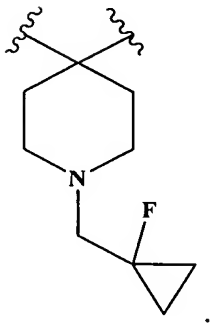
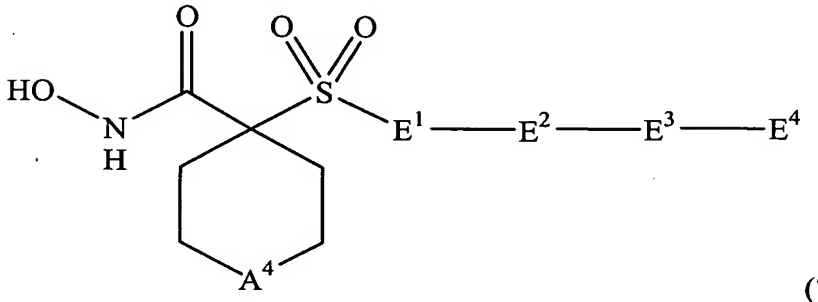

, and

.

7. A compound or salt thereof according to claim 5, wherein:

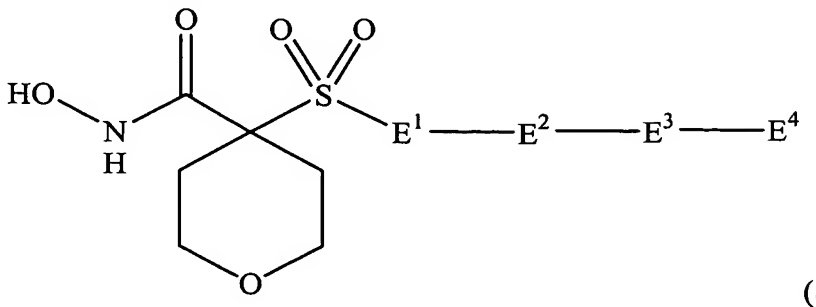
the compound corresponds in structure to Formula (7-1):



(7-1); and

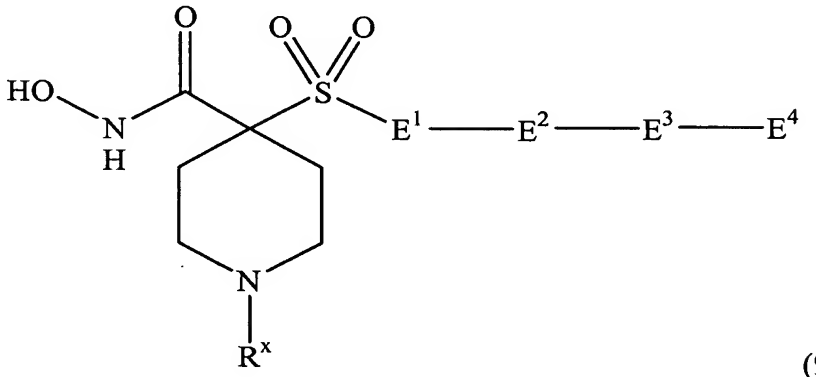
A^4 is selected from the group consisting of $-C(H)_2-$, $-C(R^x)(H)-$, $-C(R^x)_2-$, -O-, $-N(H)-$, $-N(R^x)-$, -S-, -S(O)-, and $-S(O)_2-$.

8. A compound or salt thereof according to claim 7, wherein the compound corresponds in structure to Formula (8-1):



(8-1).

9. A compound or salt thereof according to claim 7, wherein the compound corresponds in structure to Formula (9-1):



(9-1).

10. A compound or salt thereof according to claim 7, wherein E^2 is phenyl, wherein the phenyl optionally is substituted with one or more independently selected R^x substituents.

11. A compound or salt thereof according to claim 7, wherein E^1 is selected from the group consisting of furanyl, thienyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, thiodiazolyl, oxadiazolyl, pyrrolyl, pyrazolyl, imidazolyl, triazolyl, tetrazolyl, oxathiazolyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, triazinyl, oxathiazinyl, oxepinyl, thiepinyl, benzofuranyl, isobenzofuranyl, benzoxazolyl, benzoisoxazolyl, anthranilyl, benzothienyl, isobenzothienyl, benzothiazolyl, benzoisothiazolyl, benzothiadiazolyl, indolizinyl, pyranopyrrolyl, benzoxadiazolyl, indolyl, isoindazolyl, benzoimidazolyl, benzotriazolyl, purinyl, imidazopyrazinyl,

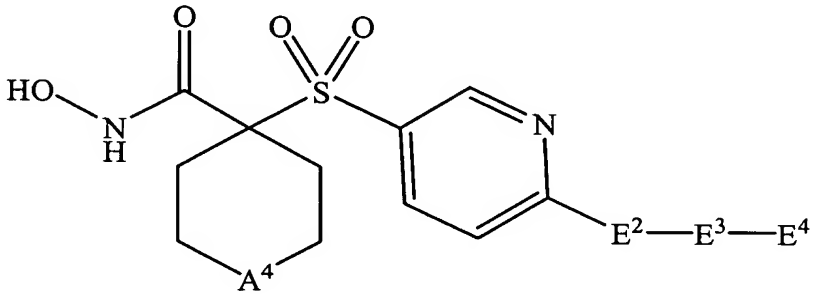
imidazolopyridazyl, quinolinyl, isoquinolinyl, pyridopyridinyl, phthalazinyl, quinoxalinyl, benzodiazinyl, pteridinyl, pyridazinotetrazinyl, pyrazinotetrazinyl, pyrimidinotetrazinyl, benzoimidazothiazolyl, carbazolyl, and acridinyl, wherein:

any member of such group optionally is substituted with one or more independently selected R^x substituents.

12. A compound or salt thereof according to claim 11, wherein E^1 is a 5-member ring.

13. A compound or salt thereof according to claim 11, wherein E^1 is a 6-member ring.

14. A compound or salt thereof according to claim 13, wherein the compound corresponds in structure to Formula (14-1):

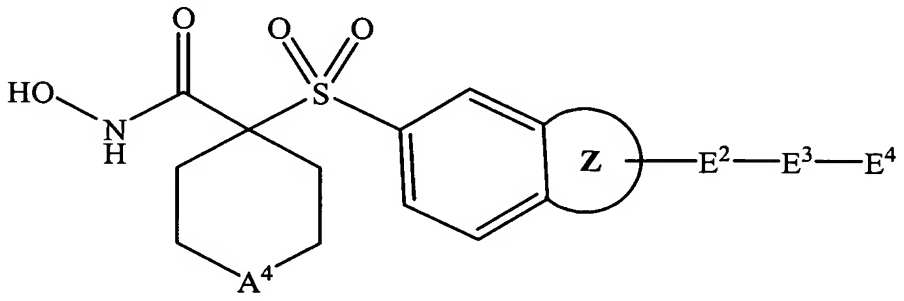


(14-1).

15. A compound or salt thereof according to claim 11, wherein E^1 is a 9-member fused-ring structure.

16. A compound or salt thereof according to claim 15, wherein:

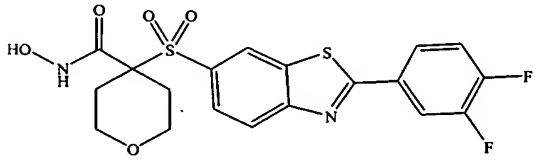
the compound corresponds in structure to Formula (16-1):



(16-1), and

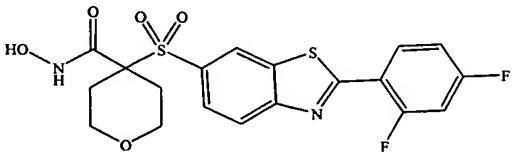
the Z-ring is a 5-member ring.

17. A compound or salt thereof according to claim 16, wherein the compound corresponds in structure to a formula selected from the group consisting of:



(17-1)

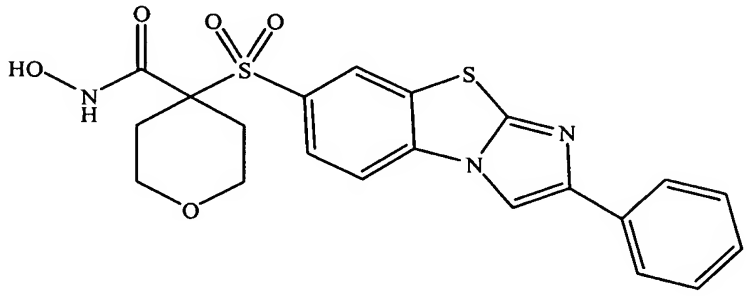
and



(17-2).

18. A compound or salt thereof according to claim 11, wherein E^1 is a 12-member fused-ring structure.

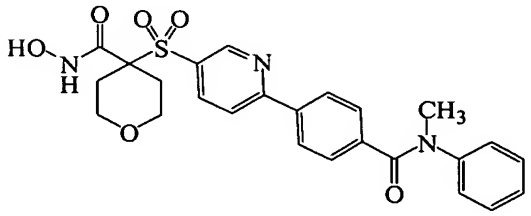
19. A compound or salt thereof according to claim 18, wherein the compound corresponds in structure to Formula (19-1):



(19-1).

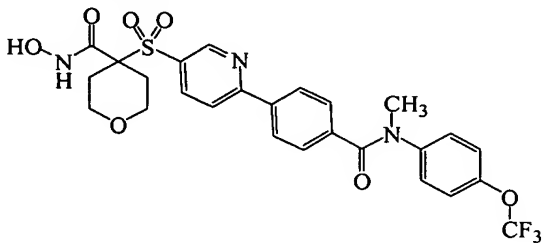
20. A compound or salt thereof according to claim 7, wherein E^4 is carbocyclyl optionally substituted with one or more independently selected R^d substituents.

21. A compound or salt thereof according to claim 20, wherein the compound corresponds in structure to a formula selected from the group consisting of:



(21-1)

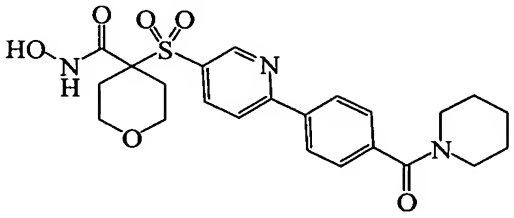
and



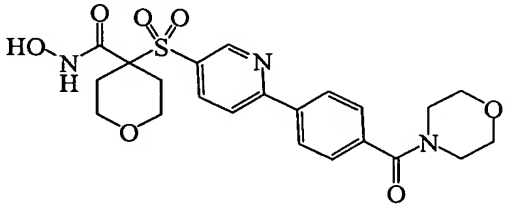
(21-2).

22. A compound or salt thereof according to claim 7, wherein E^4 is heterocyclyl optionally substituted with one or more independently selected R^d substituents.

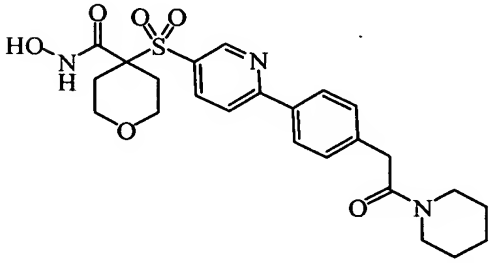
23. A compound or salt thereof according to claim 22, wherein the compound corresponds in structure to a formula selected from the group consisting of:



(23-1),



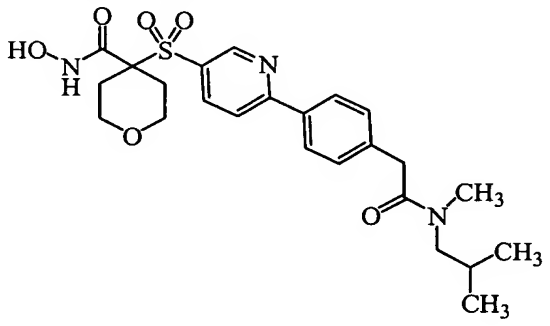
(23-2), and



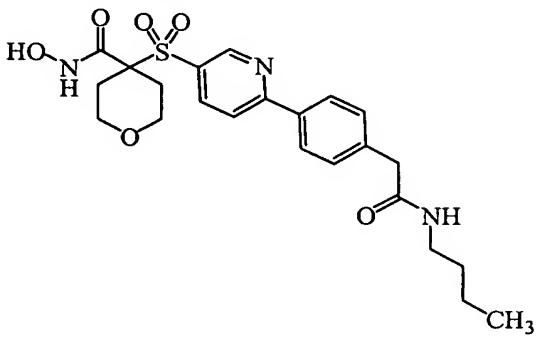
(23-3).

24. A compound or salt thereof according to claim 7, wherein E^4 is aminoalkyl optionally substituted with one or more independently selected R^d substituents.

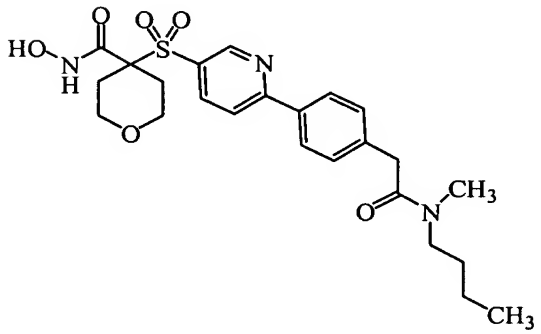
25. A compound or salt thereof according to claim 24, wherein the compound corresponds in structure to a formula selected from the group consisting of:



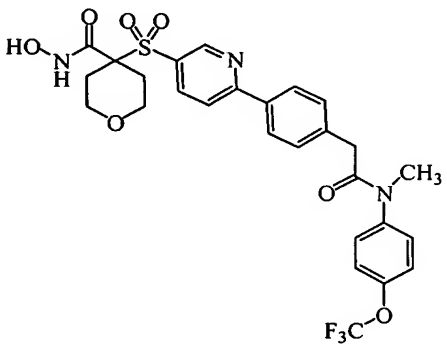
(25-1),



(25-2),



(25-3), and



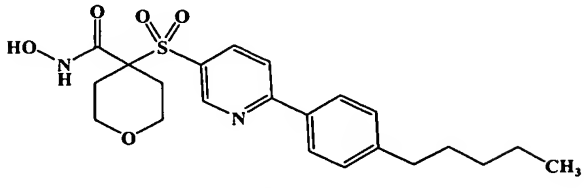
(25-4).

26. A compound or salt thereof according to claim 7, wherein E^4 is selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxyalkyl, alkoxyalkoxyalkyl, alkylthioalkyl, alkylthioalkylthioalkyl, alkylthioalkoxyalkyl, alkoxyalkylthioalkyl, and aminoalkyl, wherein:

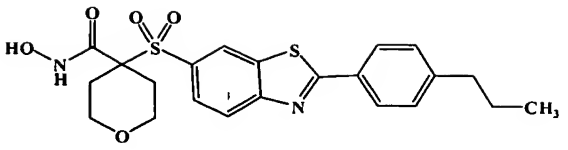
any member of such group optionally is substituted with one or more independently selected halogen.

27. A compound or salt thereof according to claim 26, wherein E^3 is selected from the group consisting of a bond, -O-, -C(O)-N(H)-, -C(O)-$N(CH_3)$-, and -C(O)-$N(CH_2CH_3)$-.

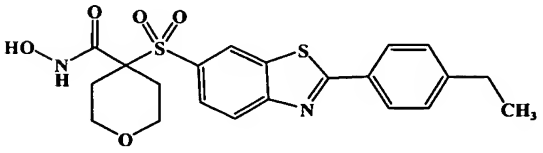
28. A compound or salt thereof according to claim 27, wherein the compound corresponds in structure to a formula selected from the group consisting of:



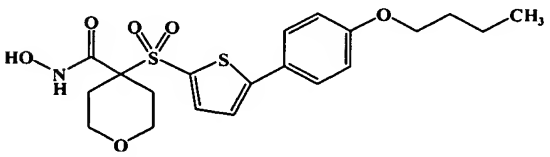
(28-1),



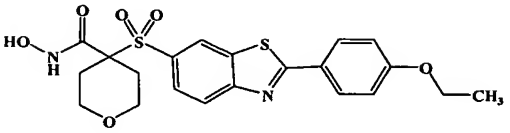
(28-2),



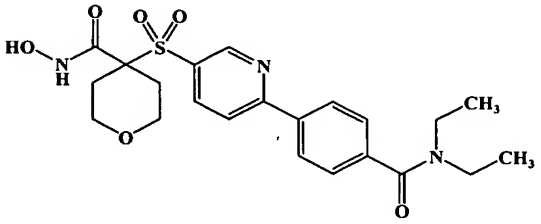
(28-3),



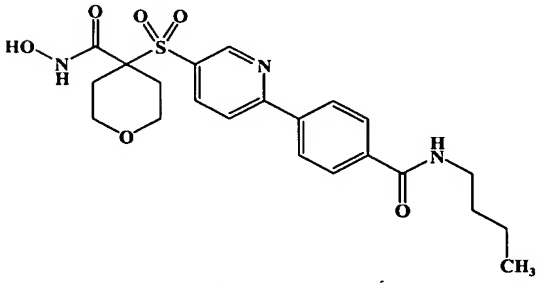
(28-4)



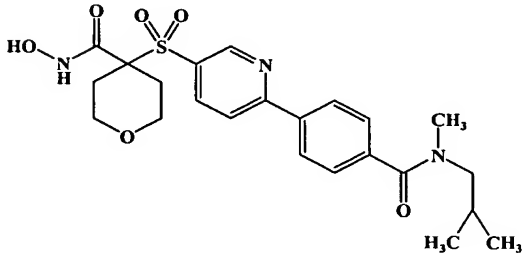
(28-5).



(28-6),



(28-7), and



(28-8).

29. A compound or salt thereof according to claim 26, wherein E^4 is C_1-C_6-alkyl substituted with one or more fluoro.

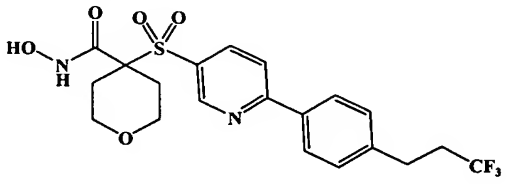
30. A compound or salt thereof according to claim 29, wherein E^4 is selected from the group consisting of:

trifluoromethyl, and

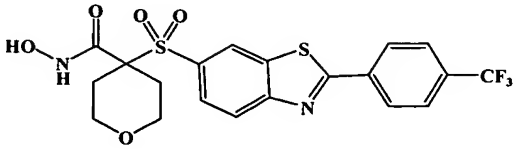
C_1-C_5-alkyl substituted with trifluoromethyl.

31. A compound or salt thereof according to claim 30, wherein E^3 is selected from the group consisting of a bond, -O-, and -S-.

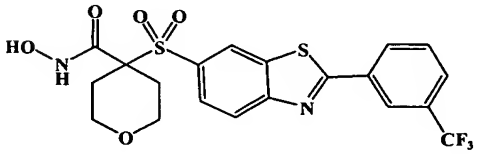
32. A compound or salt thereof according to claim 31, wherein the compound is selected from the group consisting of:



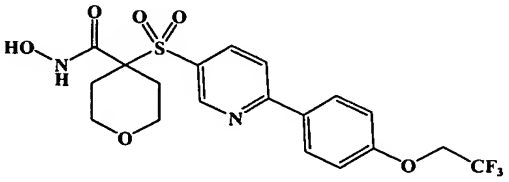
(32-1),



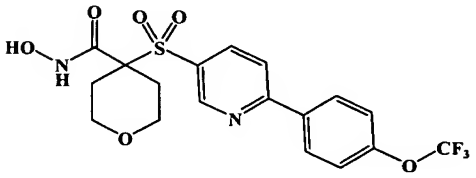
(32-2),



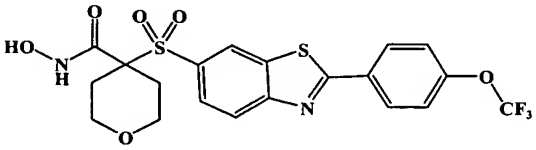
(32-3),



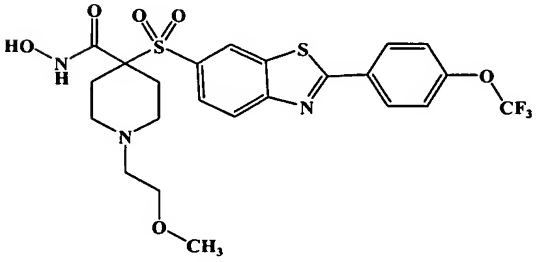
(32-4),



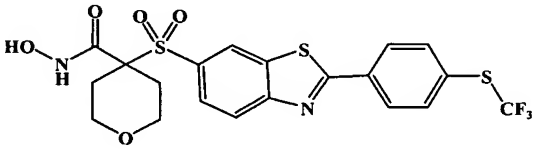
(32-5),



(32-6),



(32-7), and



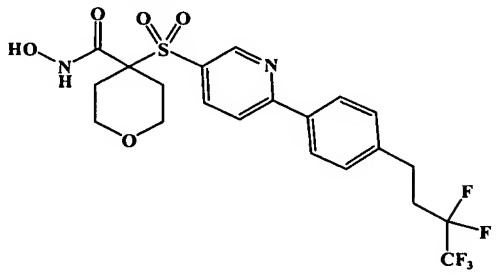
(32-8).

33. A compound or salt thereof according to claim 29, wherein E^4 is selected from the group consisting of:

pentafluoroethyl, and

C_1-C_4-alkyl substituted with pentafluoroethyl.

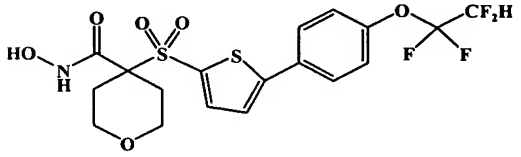
34. A compound or salt thereof according to claim 33, wherein the compound corresponds in structure to Formula (34-1):



(34-1).

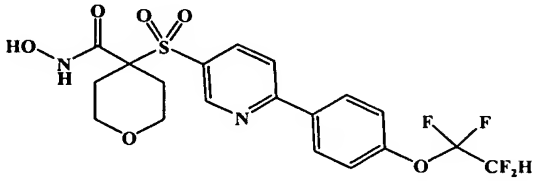
35. A compound or salt thereof according to claim 29, wherein E^4 is C_1-C_6-alkyl comprising a carbon atom bonded to at least one hydrogen and at least one fluoro.

36. A compound or salt thereof according to claim 35, wherein the compound corresponds in structure to a formula selected from the group consisting of:



(36-1)

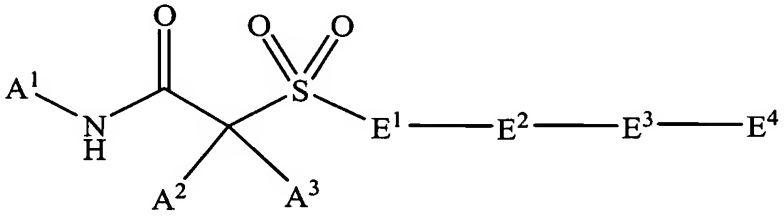
and



(36-2).

37. A compound or a salt thereof, wherein:

the compound corresponds in structure to Formula 37-1:



(37-1); and

A^1 is selected from the group consisting of hydrogen, hydroxyl, carbocyclyloxy, and heterocyclyloxy; and

as to A^2 and A^3:

A^2 and A^3, together with the carbon to which they are both bonded, form heterocyclyl or carbocyclyl, wherein:

the heterocyclyl or carbocyclyl optionally is substituted with up to 3 independently selected R^X substituents, and

the heterocyclyl or carbocyclyl optionally is substituted with two substituents such that the two substituents, together with the atom(s) to which they are bonded, form a carbocyclyl or heterocyclyl, wherein:

the optional heterocyclyl or carbocyclyl substituent is, in turn, optionally substituted with up to 3 independently selected R^X substituents, or

A^2 and A^3 are independently selected from the group consisting of hydrogen, alkyl, alkoxyalkyl, alkylthioalkyl, alkenyl, alkynyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkenyl, carbocyclylalkynyl, carbocyclyloxyalkyl, carbocyclylalkoxyalkyl, carbocyclylalkylthio, carbocyclylthioalkyl, carbocyclylalkylthioalkyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, heterocyclyloxyalkyl, heterocyclylalkoxyalkyl, heterocyclylalkylthio, heterocyclylthioalkyl, and heterocyclylalkylthioalkyl, wherein:

any member of such group optionally is substituted with up to 3 independently selected R^X substituents, and

any member of such group optionally is substituted with two substituents such that the two substituents, together with the atom(s) to which they are bonded, form a carbocyclyl or heterocyclyl, wherein:

the optional heterocyclyl or carbocyclyl is, in turn, optionally substituted with up to 3 independently selected R^X substituents; and

E^1 is selected from the group consisting of furanyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, thiodiazolyl, oxadiazolyl, pyrrolyl, pyrazolyl, imidazolyl, triazolyl, tetrazolyl, oxathiazolyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, triazinyl, oxathiazinyl, oxepinyl, thiepinyl, benzofuranyl, isobenzofuranyl, benzoxazolyl, benzoisoxazolyl, anthranilyl, benzothienyl, isobenzothienyl, benzothiazolyl, benzoisothiazolyl, benzothiadiazolyl, indolizinyl, pyranopyrrolyl, benzoxadiazolyl, indolyl, isoindazolyl, benzoimidazolyl, benzotriazolyl, purinyl,

imidazopyrazinyl, imidazolopyridazyl, quinolinyl, isoquinolinyl, pyridopyridinyl, phthalazinyl, quinoxalinyl, benzodiazinyl, pteridinyl, pyridazinotetrazinyl, pyrazinotetrazinyl, pyrimidinotetrazinyl, benzoimidazothiazolyl, carbazolyl, and acridinyl, wherein:

any member of such group optionally is substituted with one or more independently selected R^x substituents; and

E^2 is heterocyclyl, wherein the heterocyclyl optionally is substituted with one or more independently selected R^x substituents; and

E^3 is absent or selected from the group consisting of -O-, -C(O)-, -C(O)-O-, -O-C(O)-, -N(R^b)-, -C(O)-N(R^b)-, -N(R^b)-C(O)-, -C(O)-N(R^b)-N(R^b)-C(O)-, -N(R^b)-C(O)-N(R^b)-, -S-, -S(O)-, -S(O)$_2$-, -N(R^b)-S(O)$_2$-, -S(O)$_2$-N(R^b)-, -O-S(O)$_2$-, -S(O)$_2$-O-, -C(NH)-, -C(NOH)-, -N(R^b)-C(NH)-, -N(R^b)-C(NOH)-, -C(NH)-N(R^b)-, -C(NOH)-N(R^b)-, alkyl, alkenyl, carbonylalkyl, alkylcarbonyl, and a bond, wherein:

any alkyl or alkenyl portion of a substituent in such group optionally is substituted with one or more independently selected R^c substituents; and

E^4 is absent or selected from the group consisting of hydrogen, halogen, cyano, alkyl, alkenyl, alkynyl, alkoxyalkyl, alkoxyalkoxyalkyl, alkylthioalkyl, alkylthioalkylthioalkyl, alkylthioalkoxyalkyl, alkoxyalkylthioalkyl, aminoalkyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkoxyalkyl, heterocyclyl, heterocyclylalkyl, and heterocyclylalkoxyalkyl, wherein:

any member of such group optionally is substituted with one or more independently selected R^d substituents; and

each R^x is independently selected from the group consisting of halogen, cyano, hydroxy, nitro, nitroso, oxo, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkoxy, R^b-oxyalkyl, alkenyloxy, alkynyloxy, alkylthio, R^bR^b-amino, R^bR^b-aminoalkyl, R^bR^b-aminoalkoxy, R^bR^b-aminoalkyl(R^b)amino, carbocyclyl, carbocyclylalkyl, carbocyclyloxy, carbocyclyloxyalkoxy, carbocyclylthio, heterocyclyl, heterocyclylalkyl, heterocyclyloxy, heterocyclyloxyalkoxy, heterocyclylthio, alkyliminocarbonyl, alkylthioalkyl, alkylsulfonylalkyl, alkylsulfoxidoalkyl, alkylthioalkenyl, alkylsulfoxidoalkenyl, alkylsulfonylalkenyl, carbocyclylalkoxyalkyl, carbocyclyliminocarbonyl, carbocyclylthioalkyl, carbocyclylsulfoxidoalkyl,

carbocyclylsulfonylalkyl, carbocyclylthioalkenyl, carbocyclylsulfoxidoalkenyl, carbocyclylsulfonylalkenyl, heterocyclylalkoxyalkyl, heterocyclylthioalkyl, heterocyclylsulfoxidoalkyl, heterocyclylsulfonylalkyl, heterocyclylthioalkenyl, heterocyclylsulfoxidoalkenyl, heterocyclylsulfonylalkenyl, heterocyclyliminocarbonyl, aminosulfonylalkyl, and $-R^{x1}-R^{x2}$, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, amino, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, and alkyl; and

each R^{x1} is selected from the group consisting of -C(O)-, -C(S)-, $-C(NR^y)-$, -S(O)-, and $-S(O)_2-$; and

each R^y is selected from the group consisting of hydrogen and hydroxy; and

each R^{x2} is selected from the group consisting of hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, alkoxyalkoxy, R^b-oxyalkyl, alkenyloxy, alkynyloxy, R^bR^b-amino, R^bR^b-aminoalkyl, R^bR^b-aminoalkoxy, R^bR^b-aminoalkyl(R^b)amino, carbocyclyl, carbocyclylalkyl, carbocyclyloxy, carbocyclyloxyalkoxy, heterocyclyl, heterocyclylalkyl, heterocyclyloxy, and heterocyclyloxyalkoxy, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen and hydroxy; and

each R^b is independently selected from the group consisting of hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, bisalkoxyalkyl, alkylthioalkyl, alkylthioalkenyl, alkylsulfoxidoalkyl, alkylsulfonyl, alkylsulfonylalkyl, carbocyclyl,

carbocyclylalkyl, carbocyclyloxyalkyl, carbocyclylalkoxyalkyl, carbocyclylthioalkyl, carbocyclylthioalkenyl, carbocyclylsulfoxidoalkyl, carbocyclylsulfonyl, carbocyclylsulfonylalkyl, heterocyclyl, heterocyclylalkyl, heterocyclyloxyalkyl, heterocyclylalkoxyalkyl, heterocyclylthioalkyl, heterocyclylsulfoxidoalkyl, heterocyclylsulfonyl, heterocyclylsulfonylalkyl, aminoalkyl, aminosulfonyl, aminoalkylsulfonyl, and alkoxyalkylaminoalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkylcarbonyl, carbocyclyl, and carbocyclylalkyl; and

each R^c is independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, -C(H)(NH), -C(H)(NOH), thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, amino, alkyl, alkoxy, alkenyl, alkynyl, alkoxyalkyl, mono-alkylamino, di-alkylamino, alkylthio, carbocyclyl, carbocyclylalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, amino, alkyl, and carbocyclylalkyl; and

each R^d is independently selected from the group consisting of halogen, hydroxy, cyano, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, $-N(R^e)_2$, $-C(O)(R^f)$, $-S-R^e$, $-S(O)_2-R^e$, carbocyclyl, alkylcarbocyclyl, alkoxycarbocyclyl, carbocyclylalkyl, heterocyclyl, alkylheterocyclyl, alkylheterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

each R^e is independently selected from the group consisting of hydrogen alkyl, carbocyclyl, carbocyclylalkyl, heterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen,

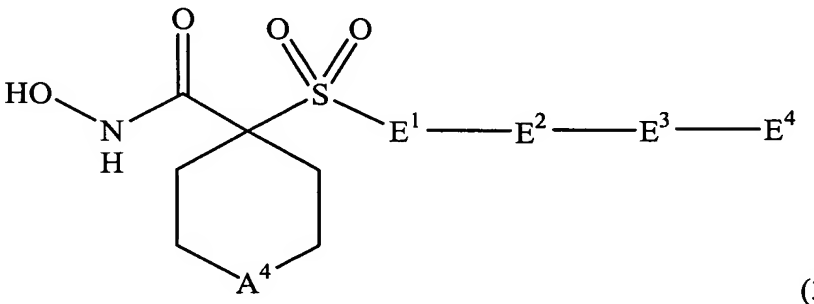
hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

each R^f is independently selected from the group consisting of hydrogen, alkyl, -O-R^e, -N(R^e)$_2$, carbocyclylalkyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino.

38. A compound or salt thereof according to claim 37, wherein:

the compound corresponds in structure to Formula (38-1):



(38-1); and

A^4 is selected from the group consisting of C(H)$_2$-, -C(R^x)(H)-, -C(R^x)$_2$-, -O-, -N(H)-, -N(R^x)-, -S-, -S(O)-, and -S(O)$_2$-.

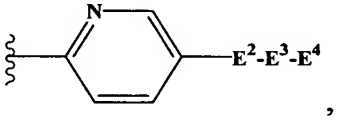
39. A compound or salt thereof according to claim 38, wherein E^1 is selected from the group consisting of oxazolyl, isoxazolyl, isothiazolyl, thiodiazolyl, oxadiazolyl, pyrrolyl, pyrazolyl, triazolyl, tetrazolyl, oxathiazolyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, triazinyl, oxathiazinyl, oxepinyl, thiepinyl, benzofuranyl, isobenzofuranyl, benzoisoxazolyl, anthranilyl, benzothienyl, isobenzothienyl, benzoisothiazolyl, benzothiadiazolyl, indolizinyl, pyranopyrrolyl, benzoxadiazolyl, indolyl, isoindazolyl, benzoimidazolyl, benzotriazolyl, purinyl, imidazopyrazinyl, imidazolopyridazyl, isoquinolinyl, pyridopyridinyl, phthalazinyl, quinoxalinyl, benzodiazinyl, pteridinyl, pyridazinotetrazinyl, pyrazinotetrazinyl, pyrimidinotetrazinyl, benzoimidazothiazolyl, carbazolyl, and acridinyl, wherein:

any member of such group optionally is substituted with one or more independently selected R^x substituents.

40. A compound or salt thereof according to claim 38, wherein E^1 is 5-member heteroaryl, wherein the heteroaryl optionally is substituted with one or more independently selected R^x substituents.

41. A compound or salt thereof according to claim 38, wherein E^1 is 6-member heteroaryl, wherein the heteroaryl optionally is substituted with one or more independently selected R^x substituents.

42. A compound or salt thereof according to claim 41, wherein $-E^1-E^2-E^3-E^4$ corresponds in structure to a formula selected from the group consisting of: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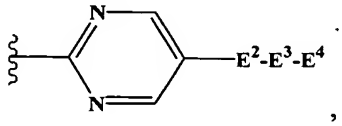
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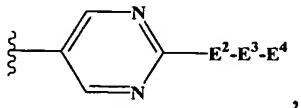
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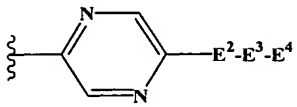
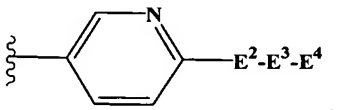

, and

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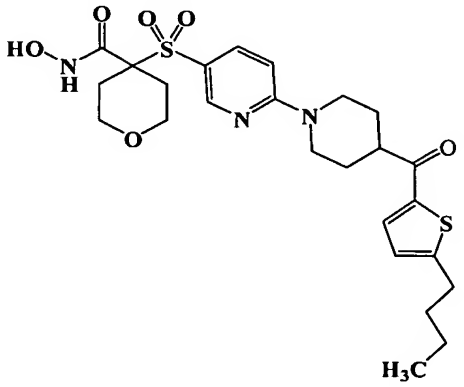
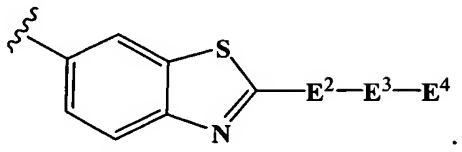
43. A compound or salt thereof according to claim 42, wherein the compound corresponds in structure to Formula (43-1):


(43-1).

44. A compound or salt thereof according to claim 38, wherein $-E^1-E^2-E^3-E^4$ corresponds in structure to the following formula:



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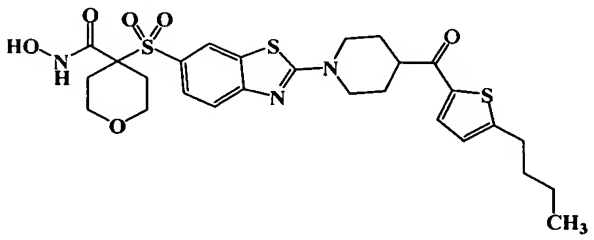
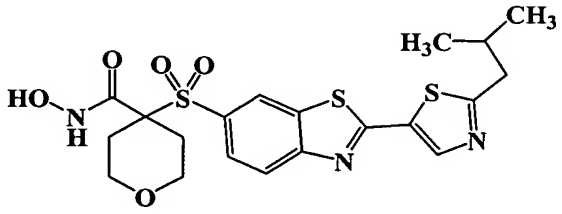
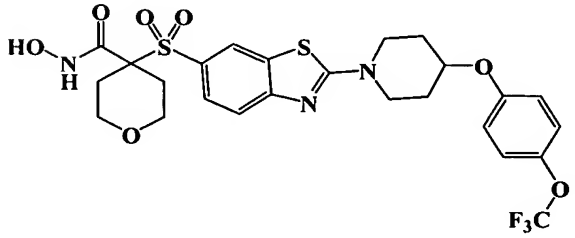
45. A compound or salt thereof according to claim 44, wherein the compound corresponds in structure to a formula selected from the group consisting of:



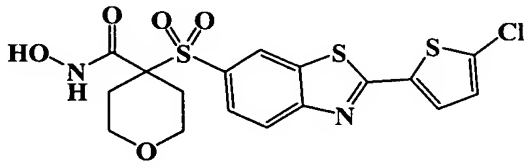
(45-1),



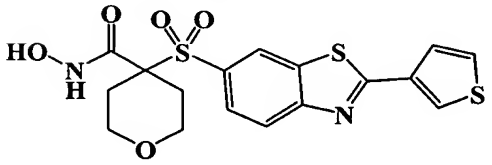
(45-2),



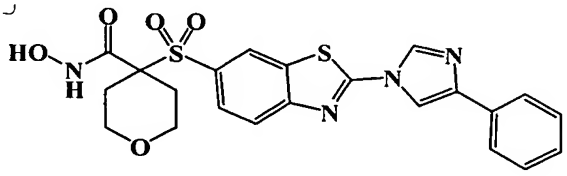
(45-3),



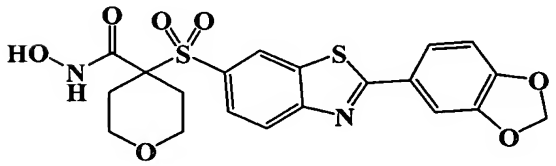
(45-4),



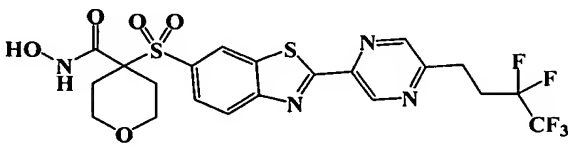
(45-5),



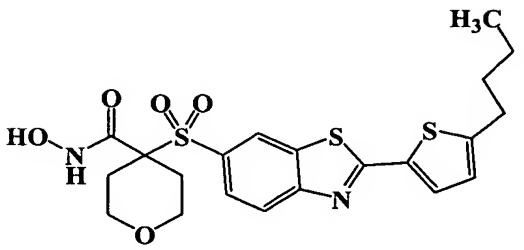
(45-6),



(45-7),



(45-8), and

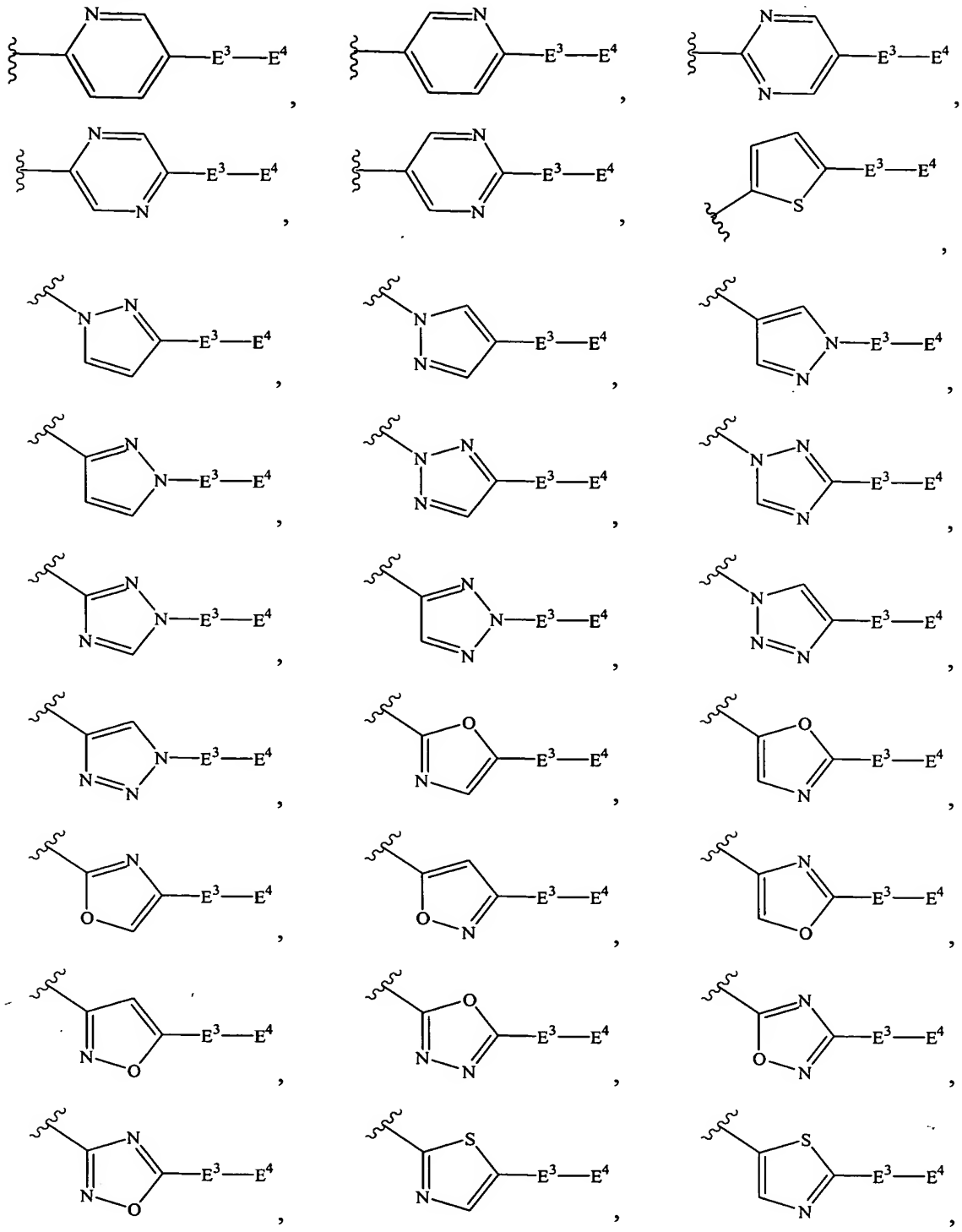


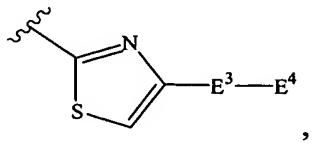
(45-9).

46. A compound or salt thereof according to claim 38, wherein E^2 is selected from the group consisting of furanyl, thienyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, thiodiazolyl, oxadiazolyl, pyrrolyl, pyrazolyl, imidazolyl, triazolyl, tetrazolyl, oxathiazolyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, triazinyl, oxathiazinyl, oxepinyl, thiepinyl, benzofuranyl, isobenzofuranyl, benzoxazolyl, benzoisoxazolyl, anthranilyl, benzothienyl, isobenzothienyl, benzothiazolyl, benzoisothiazolyl, benzothiadiazolyl, indolizinyl, pyranopyrrolyl, benzoxadiazolyl, indolyl, isoindazolyl, benzoimidazolyl, benzotriazolyl, purinyl, imidazopyrazinyl, imidazolopyridazyl, quinolinyl, isoquinolinyl, pyridopyridinyl, phthalazinyl, quinoxalinyl, benzodiazinyl, pteridinyl, pyridazinotetrazinyl, pyrazinotetrazinyl, pyrimidinotetrazinyl, benzoimidazothiazolyl, carbazolyl, acridinyl, oxatriazolyl, dihydrofuranyl, tetrahydrofuranyl, dihydrothienyl, tetrahydrothienyl, isopyrrolyl, pyrrolinyl, pyrrolidinyl, isoimidazolyl, imidazolinyl, imidazolidinyl, pyrazolinyl, pyrazolidinyl, dithiolyl, oxathiolyl, oxathiolanyl, oxazolidinyl, isoxazolidinyl, thiazolinyl, isothiazolinyl, thiazolidinyl, isothiazolidinyl, dioxazolyl, pyranyl, dihydropyranyl, tetrahydropyranyl, piperidinyl, piperazinyl, oxazinyl, isoxazinyl, oxadiazinyl, morpholinyl, azepinyl, diazepinyl, pyrindinyl, isoindolyl, indoleninyl, pyrazolopyrimidinyl, pyrazolopyrazinyl, pyrazolopyridazyl, benzodioxolyl, chromanyl, isochromanyl, thiochromanyl, isothiochromanyl, chromenyl, isochromenyl, thiochromenyl, isothiochromenyl, benzodioxanyl, tetrahydroisoquinolinyl, 4H-quinolizinyl, benzoxazinyl, benzoisoxazinyl, benzoxadiazinyl, and xanthenyl, wherein:

any member of such group is optionally substituted with one or more independently selected R^x substituents.

47. A compound or salt thereof according to claim 46, wherein $-E^2-E^3-E^4$ is selected from the group consisting of:

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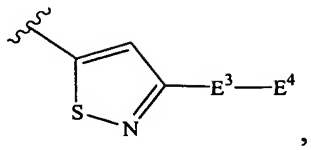
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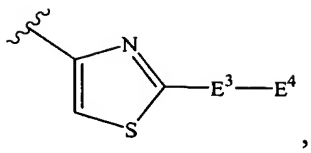
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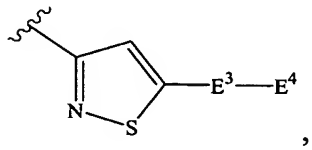
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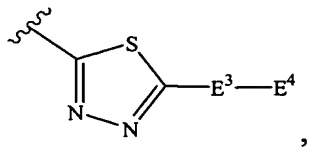
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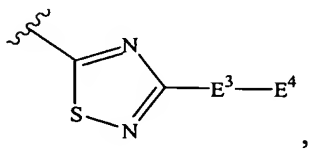
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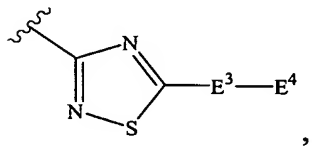
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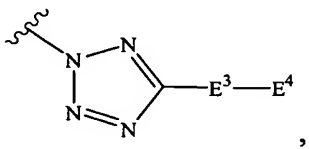
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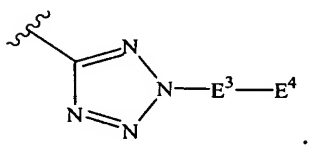
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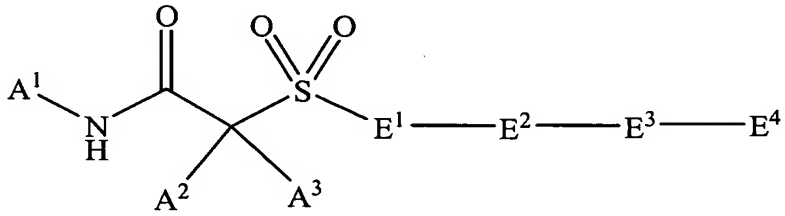
48. A compound or salt thereof according to claim 38, wherein E^2 is 5-member heterocyclyl, wherein the heterocyclyl optionally is substituted with one or more independently selected R^x substituents.

49. A compound or salt thereof according to claim 38, wherein E^2 is 6-member heterocyclyl, wherein the heterocyclyl optionally is substituted with one or more independently selected R^x substituents.

50. A compound or a salt thereof, wherein:

the compound corresponds in structure to Formula 50-1:


(50-1); and

A^1 is selected from the group consisting of hydrogen, hydroxyl, carbocyclyloxy, and heterocyclyloxy; and

as to A^2 and A^3:

A^2 and A^3, together with the carbon to which they are both bonded, form heterocyclyl or carbocyclyl, wherein:

the heterocyclyl or carbocyclyl optionally is substituted with up to 3 independently selected R^X substituents, and

the heterocyclyl or carbocyclyl optionally is substituted with two substituents such that the two substituents, together with the atom(s) to which they are bonded, form a carbocyclyl or heterocyclyl, wherein:

the optional heterocyclyl or carbocyclyl substituent is, in turn, optionally substituted with up to 3 independently selected R^X substituents, or

A^2 and A^3 are independently selected from the group consisting of hydrogen, alkyl, alkoxyalkyl, alkylthioalkyl, alkenyl, alkynyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkenyl, carbocyclylalkynyl, carbocyclyloxyalkyl, carbocyclylalkoxyalkyl, carbocyclylalkylthio, carbocyclylthioalkyl, carbocyclylalkylthioalkyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, heterocyclyloxyalkyl, heterocyclylalkoxyalkyl, heterocyclylalkylthio, heterocyclylthioalkyl, and heterocyclylalkylthioalkyl, wherein:

any member of such group optionally is substituted with up to 3 independently selected R^X substituents, and

any member of such group optionally is substituted with two substituents such that the two substituents, together with the atom(s) to which they are bonded, form a carbocyclyl or heterocyclyl, wherein:

the optional heterocyclyl or carbocyclyl is, in turn, optionally substituted with up to 3 independently selected R^X substituents; and

E^1 is heteroaryl, wherein the heteroaryl optionally is substituted with one or more independently selected R^x substituents; and

E^2 is selected from the group consisting of carbocyclyl and heterocyclyl, wherein:

the carbocyclyl and heterocyclyl optionally are substituted with one or more independently selected R^x substituents; and

E^3 is selected from the group consisting of -O-, -C(O)-, -C(O)-O-, -O-C(O)-, -N(R^b)-, -C(O)-N(R^b)-, -N(R^b)-C(O)-, -C(O)-N(R^b)-N(R^b)-C(O)-, -N(R^b)-C(O)-N(R^b)-, -S-, -S(O)-, -S(O)$_2$-, -N(R^b)-S(O)$_2$-, -S(O)$_2$-N(R^b)-, -O-S(O)$_2$-, -S(O)$_2$-O-, -C(NH)-, -C(NOH)-, -N(R^b)-C(NH)-, -N(R^b)-C(NOH)-, -C(NH)-N(R^b)-, -C(NOH)-N(R^b)-, alkyl, alkenyl, carbonylalkyl, alkylcarbonyl, and a bond, wherein:

any alkyl or alkenyl portion of a substituent in such group optionally is substituted with one or more independently selected R^c substituents; and

E^4 is selected from the group consisting of halogen, cyano, alkyl, alkenyl, alkynyl, alkoxyalkyl, alkoxyalkoxyalkyl, alkylthioalkyl, alkylthioalkylthioalkyl, alkylthioalkoxyalkyl, alkoxyalkylthioalkyl, aminoalkyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkoxyalkyl, heterocyclyl, heterocyclylalkyl, and heterocyclylalkoxyalkyl, wherein:

any member of such group optionally is substituted with one or more independently selected R^d substituents; and

each R^x is independently selected from the group consisting of halogen, cyano, hydroxy, nitro, nitroso, oxo, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkoxy, R^b-oxyalkyl, alkenyloxy, alkynyloxy, alkylthio, R^bR^b-amino, R^bR^b-aminoalkyl, R^bR^b-aminoalkoxy, R^bR^b-aminoalkyl(R^b)amino, carbocyclyl, carbocyclylalkyl, carbocyclyloxy, carbocyclyloxyalkoxy, carbocyclylthio, heterocyclyl, heterocyclylalkyl, heterocyclyloxy, heterocyclyloxyalkoxy, heterocyclylthio, alkyliminocarbonyl, alkylthioalkyl, alkylsulfonylalkyl, alkylsulfoxidoalkyl, alkylthioalkenyl, alkylsulfoxidoalkenyl, alkylsulfonylalkenyl, carbocyclylalkoxyalkyl, carbocyclyliminocarbonyl, carbocyclylthioalkyl, carbocyclylsulfoxidoalkyl, carbocyclylsulfonylalkyl, carbocyclylthioalkenyl, carbocyclylsulfoxidoalkenyl, carbocyclylsulfonylalkenyl, heterocyclylalkoxyalkyl, heterocyclylthioalkyl, heterocyclylsulfoxidoalkyl, heterocyclylsulfonylalkyl, heterocyclylthioalkenyl, heterocyclylsulfoxidoalkenyl, heterocyclylsulfonylalkenyl, heterocyclyliminocarbonyl, aminosulfonylalkyl, and -R^{x1}-R^{x2}, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen,

hydroxy, cyano, amino, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, and alkyl; and

each R^{x1} is selected from the group consisting of -C(O)-, -C(S)-, -C(NR^y)-, -S(O)-, and -$S(O)_2$-; and

each R^y is selected from the group consisting of hydrogen and hydroxy; and

each R^{x2} is selected from the group consisting of hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, alkoxyalkoxy, R^b-oxyalkyl, alkenyloxy, alkynyloxy, R^bR^b-amino, R^bR^b-aminoalkyl, R^bR^b-aminoalkoxy, R^bR^b-aminoalkyl(R^b)amino, carbocyclyl, carbocyclylalkyl, carbocyclyloxy, carbocyclyloxyalkoxy, heterocyclyl, heterocyclylalkyl, heterocyclyloxy, and heterocyclyloxyalkoxy, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen and hydroxy; and

each R^b is independently selected from the group consisting of hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, bisalkoxyalkyl, alkylthioalkyl, alkylthioalkenyl, alkylsulfoxidoalkyl, alkylsulfonyl, alkylsulfonylalkyl, carbocyclyl, carbocyclylalkyl, carbocyclyloxyalkyl, carbocyclylalkoxyalkyl, carbocyclylthioalkyl, carbocyclylthioalkenyl, carbocyclylsulfoxidoalkyl, carbocyclylsulfonyl, carbocyclylsulfonylalkyl, heterocyclyl, heterocyclylalkyl, heterocyclyloxyalkyl, heterocyclylalkoxyalkyl, heterocyclylthioalkyl, heterocyclylsulfoxidoalkyl, heterocyclylsulfonyl, heterocyclylsulfonylalkyl, aminoalkyl, aminosulfonyl, aminoalkylsulfonyl, and alkoxyalkylaminoalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkylcarbonyl, carbocyclyl, and carbocyclylalkyl; and

each R^c is independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, -C(H)(NH), -C(H)(NOH), thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, amino, alkyl, alkoxy, alkenyl, alkynyl, alkoxyalkyl, mono-alkylamino, di-alkylamino, alkylthio, carbocyclyl, carbocyclylalkyl, carbocyclyloxy, heterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, amino, alkyl, and carbocyclylalkyl; and

each R^d is independently selected from the group consisting of halogen, hydroxy, cyano, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, $-N(R^e)_2$, $-C(O)(R^f)$, $-S-R^e$, $-S(O)_2-R^e$, carbocyclyl, alkylcarbocyclyl, alkylcarbocyclyl, carbocyclylalkyl, heterocyclyl, alkylheterocyclyl, alkoxyheterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

each R^e is independently selected from the group consisting of hydrogen alkyl, carbocyclyl, carbocyclylalkyl, heterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

each R^f is independently selected from the group consisting of hydrogen, alkyl, $-O-R^e$, $-N(R^e)_2$, carbocyclylalkyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen,

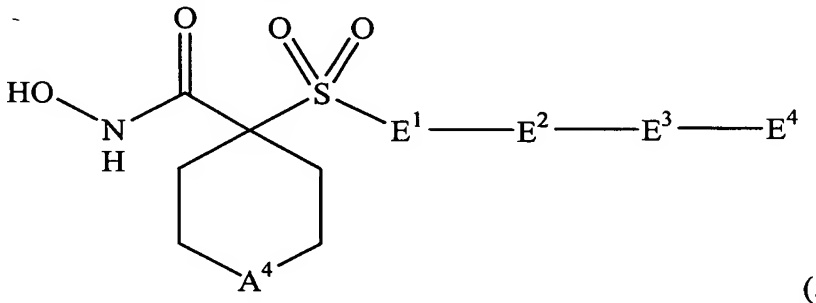
hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino.

51. A compound or salt thereof according to claim 50, wherein E^1 is selected from the group consisting of furanyl, thienyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, thiodiazolyl, oxadiazolyl, pyrrolyl, pyrazolyl, imidazolyl, triazolyl, tetrazolyl, oxathiazolyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, triazinyl, oxathiazinyl, oxepinyl, thiepinyl, benzofuranyl, isobenzofuranyl, benzoxazolyl, benzoisoxazolyl, anthranilyl, benzothienyl, isobenzothienyl, benzothiazolyl, benzoisothiazolyl, benzothiadiazolyl, indolizinyl, pyranopyrrolyl, benzoxadiazolyl, indolyl, isoindazolyl, benzoimidazolyl, benzotriazolyl, purinyl, imidazopyrazinyl, imidazolopyridazyl, quinolinyl, isoquinolinyl, pyridopyridinyl, phthalazinyl, quinoxalinyl, benzodiazinyl, pteridinyl, pyridazinotetrazinyl, pyrazinotetrazinyl, pyrimidinotetrazinyl, benzoimidazothiazolyl, carbazolyl, and acridinyl, wherein:

any member of such group optionally is substituted with one or more independently selected R^x substituents.

52. A compound or salt thereof according to claim 50, wherein:

the compound corresponds in structure to Formula (52-1):



(52-1); and

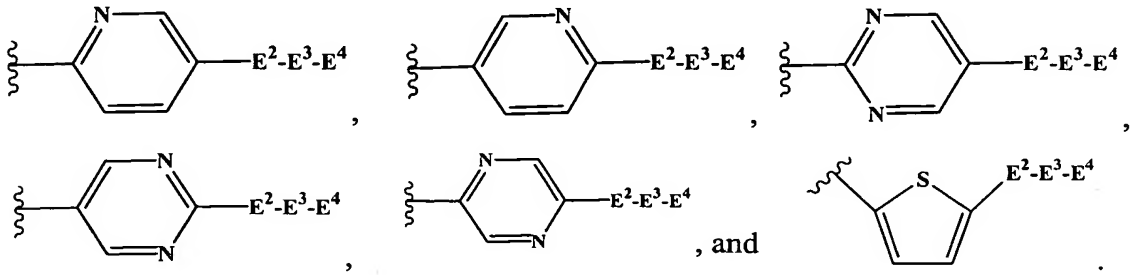
A^4 is selected from the group consisting of $-C(H)_2-$, $-C(R^x)(H)-$, $-C(R^x)_2-$, -O-, $-N(H)-$, $-N(R^x)-$, -S-, $-S(O)-$, and $-S(O)_2-$.

53. A compound or salt thereof according to claim 52, wherein E^2 is selected from the group consisting of furanyl, thienyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, thiodiazolyl, oxadiazolyl, pyrrolyl, pyrazolyl, imidazolyl, triazolyl,

tetrazolyl, oxathiazolyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, triazinyl, oxathiazinyl, oxepinyl, thiepinyl, benzofuranyl, isobenzofuranyl, benzoxazolyl, benzoisoxazolyl, anthranilyl, benzothienyl, isobenzothienyl, benzothiazolyl, benzoisothiazolyl, benzothiadiazolyl, indolizinyl, pyranopyrrolyl, benzoxadiazolyl, indolyl, isoindazolyl, benzoimidazolyl, benzotriazolyl, purinyl, imidazopyrazinyl, imidazolopyridazyl, quinolinyl, isoquinolinyl, pyridopyridinyl, phthalazinyl, quinoxalinyl, benzodiazinyl, pteridinyl, pyridazinotetrazinyl, pyrazinotetrazinyl, pyrimidinotetrazinyl, benzoimidazothiazolyl, carbazolyl, acridinyl, dihydrofuranyl, tetrahydrofuranyl, dihydrothienyl, tetrahydrothienyl, isopyrrolyl, pyrrolinyl, pyrrolidinyl, isoimidazolyl, imidazolinyl, imidazolidinyl, pyrazolinyl, pyrazolidinyl, dithiolyl, oxathiolyl, oxathiolanyl, oxazolidinyl, isoxazolidinyl, thiazolinyl, isothiazolinyl, thiazolidinyl, isothiazolidinyl, dioxazolyl, pyranyl, dihydropyranyl, tetrahydropyranyl, piperidinyl, piperazinyl, oxazinyl, isoxazinyl, oxadiazinyl, morpholinyl, azepinyl, diazepinyl, pyrindinyl, isoindolyl, indoleninyl, pyrazolopyrimidinyl, pyrazolopyrazinyl, pyrazolopyridazyl, benzodioxolyl, chromanyl, isochromanyl, thiochromanyl, isothiochromanyl, chromenyl, isochromenyl, thiochromenyl, isothiochromenyl, benzodioxanyl, tetrahydroisoquinolinyl, 4H-quinolizinyl, benzoxazinyl, benzoisoxazinyl, benzoxadiazinyl, and xanthenyl, wherein:

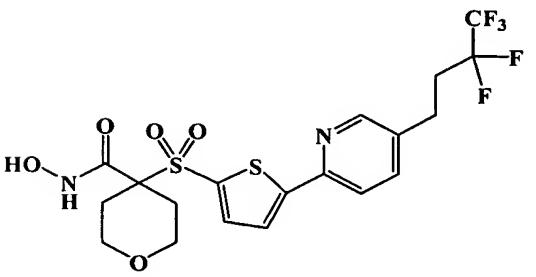
any member of such group optionally is substituted with one or more independently selected R^x substituents.

54. A compound or salt thereof according to claim 53, wherein $-E^1-E^2-E^3-E^4$ corresponds in structure to a formula selected from the group consisting of:



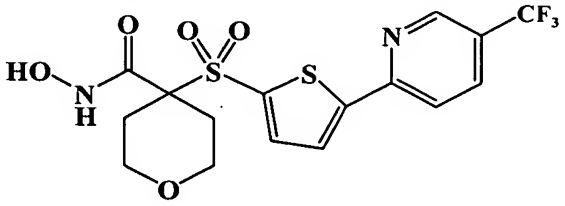
, and .

55. A compound or salt thereof according to claim 54, wherein the compound corresponds in structure to a formula selected from the group consisting of:



(55-1)

and



(55-2).

56. A method for treating a condition associated with pathologically excessive matrix metalloprotease, TNF-α convertase, or aggrecanase activity in a mammal, wherein the method comprises administering a compound (or a pharmaceutically acceptable salt thereof) recited in claim 1 to the mammal in an amount that is therapeutically effective to treat the condition.

57. A method according to claim 56, wherein A^1 is hydrogen.

58. A method according to claim 56, wherein A^1 is hydroxy.

59. A method for treating a pathological condition in a mammal, wherein:

the pathological condition is selected from the group consisting of tissue destruction, a fibrotic disease, matrix weakening, defective injury repair, a cardiovascular disease, a pulmonary disease, a kidney disease, a liver disease, an ophthalmologic disease, and a central nervous system disease; and

the method comprises administering a compound (or a pharmaceutically acceptable salt thereof) recited in claim 1 to the mammal in an amount that is therapeutically effective to treat the pathological condition.

60. A method for treating a pathological condition in a mammal, wherein:

the pathological condition is selected from the group consisting of osteoarthritis, rheumatoid arthritis, septic arthritis, tumor invasion, tumor metastasis, tumor angiogenesis, a decubitis ulcer, a gastric ulcer, a corneal ulcer, periodontal disease, liver cirrhosis, fibrotic lung disease, otosclerosis, atherosclerosis, multiple sclerosis, dilated cardiomyopathy, epidermal ulceration, epidermolysis bullosa, aortic aneurysm, defective injury repair, an adhesion, scarring, congestive heart failure, post myocardial infarction, coronary thrombosis, emphysema, proteinuria, Alzheimer's disease, bone disease, chronic obstructive pulmonary disease, and a disease of the central nervous system; and

the method comprises administering a compound (or a pharmaceutically acceptable salt thereof) recited in claim 1 to the mammal in an amount that is therapeutically effective to treat the pathological condition.

61. A method for treating a pathological condition of the central nervous system in a mammal, wherein the method comprises administering a compound (or a pharmaceutically acceptable salt thereof) recited in claim 1 to the mammal in an amount that is therapeutically effective to treat the pathological condition.

62. A pharmaceutical composition, wherein the composition comprises a therapeutically-effective amount of a compound (or a pharmaceutically acceptable salt thereof) recited in claim 1.

63. A method for treating a condition associated with pathologically excessive matrix metalloprotease, TNF-α convertase, or aggrecanase activity in a mammal, wherein the method comprises administering a compound (or a pharmaceutically acceptable salt thereof) recited in claim 37 to the mammal in an amount that is therapeutically effective to treat the condition.

64. A method according to claim 63, wherein A^1 is hydrogen.

65. A method according to claim 63, wherein A^1 is hydroxy.

66. A method for treating a pathological condition in a mammal, wherein:

the pathological condition is selected from the group consisting of tissue destruction, a fibrotic disease, matrix weakening, defective injury repair, a cardiovascular disease, a pulmonary disease, a kidney disease, a liver disease, an ophthalmologic disease, and a central nervous system disease; and

the method comprises administering a compound (or a pharmaceutically acceptable salt thereof) recited in claim 37 to the mammal in an amount that is therapeutically effective to treat the pathological condition.

67. A method for treating a pathological condition in a mammal, wherein:

the pathological condition is selected from the group consisting of osteoarthritis, rheumatoid arthritis, septic arthritis, tumor invasion, tumor metastasis, tumor angiogenesis, a decubitis ulcer, a gastric ulcer, a corneal ulcer, periodontal disease, liver cirrhosis, fibrotic lung disease, otosclerosis, atherosclerosis, multiple sclerosis, dilated cardiomyopathy, epidermal ulceration, epidermolysis bullosa, aortic aneurysm, defective injury repair, an adhesion, scarring, congestive heart failure, post myocardial infarction, coronary thrombosis, emphysema, proteinuria, Alzheimer's disease, bone disease, chronic obstructive pulmonary disease, and a disease of the central nervous system; and

the method comprises administering a compound (or a pharmaceutically acceptable salt thereof) recited in claim 37 to the mammal in an amount that is therapeutically effective to treat the pathological condition.

68. A method for treating a pathological condition of the central nervous system in a mammal, wherein the method comprises administering a compound (or a pharmaceutically acceptable salt thereof) recited in claim 37 to the mammal in an amount that is therapeutically effective to treat the pathological condition.

69. A pharmaceutical composition, wherein the composition comprises a therapeutically-effective amount of a compound (or a pharmaceutically acceptable salt thereof) recited in claim 37.

70. A method for treating a condition associated with pathologically excessive matrix metalloprotease, TNF-α convertase, or aggrecanase activity in a mammal, wherein the method comprises administering a compound (or a pharmaceutically acceptable salt thereof) recited in claim 50 to the mammal in an amount that is therapeutically effective to treat the condition.

71. A method according to claim 70, wherein A^1 is hydrogen.

72. A method according to claim 70, wherein A^1 is hydroxy.

73. A method for treating a pathological condition in a mammal, wherein:

the pathological condition is selected from the group consisting of tissue destruction, a fibrotic disease, matrix weakening, defective injury repair, a cardiovascular disease, a pulmonary disease, a kidney disease, a liver disease, an ophthalmologic disease, and a central nervous system disease; and

the method comprises administering a compound (or a pharmaceutically acceptable salt thereof) recited in claim 50 to the mammal in an amount that is therapeutically effective to treat the pathological condition.

74. A method for treating a pathological condition in a mammal, wherein:

the pathological condition is selected from the group consisting of osteoarthritis, rheumatoid arthritis, septic arthritis, tumor invasion, tumor metastasis, tumor angiogenesis, a decubitis ulcer, a gastric ulcer, a corneal ulcer, periodontal disease, liver cirrhosis, fibrotic lung disease, otosclerosis, atherosclerosis, multiple sclerosis, dilated cardiomyopathy, epidermal ulceration, epidermolysis bullosa, aortic aneurysm, defective injury repair, an adhesion, scarring, congestive heart failure, post myocardial infarction, coronary thrombosis, emphysema, proteinuria, Alzheimer's disease, bone disease, chronic obstructive pulmonary disease, and a disease of the central nervous system; and

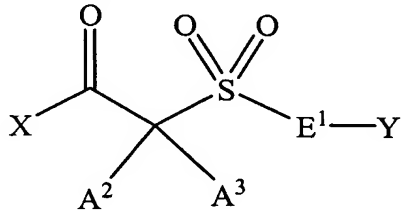
the method comprises administering a compound (or a pharmaceutically acceptable salt thereof) recited in claim 50 to the mammal in an amount that is therapeutically effective to treat the pathological condition.

75. A method for treating a pathological condition of the central nervous system in a mammal, wherein the method comprises administering a compound (or a pharmaceutically acceptable salt thereof) recited in claim 50 to the mammal in an amount that is therapeutically effective to treat the pathological condition.

76. A pharmaceutical composition, wherein the composition comprises a therapeutically-effective amount of a compound (or a pharmaceutically acceptable salt thereof) recited in claim 50.

77. A compound or a salt thereof, wherein:

the compound corresponds in structure to Formula 77-1:



(77-1); and

X is selected from the group consisting of -O-R^1, -NH-O-R^2, -NH-O-R^3, and -NR^4R^5; and

R^1 is selected from the group consisting of hydrogen, C_1-C_6-alkyl, aryl, and aryl-C_1-C_6-alkyl; and

R^2 is a selectively removable protecting group; and

R^3 is selected from the group consisting of hydrogen and C(W)R^6; and

W is selected from the group consisting of O and S; and

R^6 is selected from the group consisting of C_1-C_6-alkyl, aryl, heteroaryl-C_1-C_6-alkyl, C_3-C_8-cycloalkyl-C_1-C_6-alkyl, aryl-C_1-C_6-alkyl, heteroaryl, and amino-C_1-C_6-alkyl, wherein the amino-C_1-C_6-alkyl nitrogen optionally is substituted with:

up to two substituents independently selected from the group consisting of C_1-C_6-alkyl, aryl, aryl-C_1-C_6-alkyl, C_3-C_8-cycloalkyl-C_1-C_6-alkyl, aryl-C_1-C_6-alkoxycarbonyl, C_1-C_6-alkoxycarbonyl, and C_1-C_6-alkylcarbonyl, or

two substituents such that the amino-C_1-C_6-alkyl nitrogen and two substituents together form a 5- to 8-member heterocyclyl; and

as to R^4 and R^5:

R^4 is selected from the group consisting of hydrogen, C_1-C_6-alkyl, C_1-C_6-alkoxy, amino-C_1-C_6-alkyl, hydroxy-C_1-C_6-alkyl, aryl, aryloxy, and aryl-C_1-C_6-alkyl; and R^5 is selected from the group consisting of hydrogen, C_1-C_6-alkyl, amino-C_1-C_6-alkyl, hydroxy-C_1-C_6-alkyl, aryl, and aryl-C_1-C_6-alkyl, or

R^4 and R^5, together with the nitrogen atom to which they are both bonded, form a 5- to 8-member ring optionally comprising up to one additional heteroatom selected from the group consisting of oxygen, nitrogen, and sulfur; and

as to A^2 and A^3:

A^2 and A^3, together with the carbon to which they are both bonded, form heterocyclyl or carbocyclyl, wherein:

the heterocyclyl or carbocyclyl optionally is substituted with up to 3 independently selected R^X substituents, and

the heterocyclyl or carbocyclyl optionally is substituted with two substituents such that the two substituents, together with the atom(s) to which they are bonded, form a carbocyclyl or heterocyclyl, wherein:

the optional heterocyclyl or carbocyclyl is, in turn, optionally substituted with up to 3 independently selected R^X substituents, or

A^2 and A^3 are independently selected from the group consisting of hydrogen, alkyl, alkoxyalkyl, alkylthioalkyl, alkenyl, alkynyl, carbocyclyl,

carbocyclylalkyl, carbocyclylalkenyl, carbocyclylalkynyl, carbocyclyloxyalkyl, carbocyclylalkoxyalkyl, carbocyclylalkylthio, carbocyclylthioalkyl, carbocyclylalkylthioalkyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, heterocyclyloxyalkyl, heterocyclylalkoxyalkyl, heterocyclylalkylthio, heterocyclylthioalkyl, and heterocyclylalkylthioalkyl, wherein:

any member of such group optionally is substituted with up to 3 independently selected R^x substituents, and

any member of such group optionally is substituted with two substituents such that the two substituents, together with the atom(s) to which they are bonded, form a carbocyclyl or heterocyclyl, wherein:

the optional heterocyclyl or carbocyclyl is, in turn, optionally substituted with up to 3 independently selected R^x substituents; and

E^1 is heteroaryl, wherein the heteroaryl optionally substituted with one or more independently selected R^x substituents; and

Y is selected from the group consisting of halogen, nitro, azido, phenylsulfoxido, aryloxy, C_2-C_6-alkoxy, C_1-C_6-alkylsulfonate, arylsulfonate, and trisubstituted ammonium, wherein:

the trisubstituted ammonium substituents are independently selected from the group consisting of aryl, aryl-C_1-C_6-alkyl, and C_1-C_6-alkyl; and

each R^x is independently selected from the group consisting of halogen, cyano, hydroxy, nitro, nitroso, oxo, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkoxy, R^b-oxyalkyl, alkenyloxy, alkynyloxy, alkylthio, R^bR^b-amino, R^bR^b-aminoalkyl, R^bR^b-aminoalkoxy, R^bR^b-aminoalkyl(R^b)amino, carbocyclyl, carbocyclylalkyl, carbocyclyloxy, carbocyclyloxyalkoxy, carbocyclylthio, heterocyclyl, heterocyclylalkyl, heterocyclyloxy, heterocyclyloxyalkoxy, heterocyclylthio, alkyliminocarbonyl, alkylthioalkyl, alkylsulfonylalkyl, alkylsulfoxidoalkyl, alkylthioalkenyl, alkylsulfoxidoalkenyl, alkylsulfonylalkenyl, carbocyclylalkoxyalkyl, carbocyclyliminocarbonyl, carbocyclylthioalkyl, carbocyclylsulfoxidoalkyl, carbocyclylsulfonylalkyl, carbocyclylthioalkenyl, carbocyclylsulfoxidoalkenyl,

carbocyclylsulfonylalkenyl, heterocyclylalkoxyalkyl, heterocyclylthioalkyl, heterocyclylsulfoxidoalkyl, heterocyclylsulfonylalkyl, heterocyclylthioalkenyl, heterocyclylsulfoxidoalkenyl, heterocyclylsulfonylalkenyl, heterocyclyliminocarbonyl, aminosulfonylalkyl, and $-R^{x1}-R^{x2}$, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, amino, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, and alkyl; and

each R^{x1} is selected from the group consisting of -C(O)-, -C(S)-, $-C(NR^y)-$, -S(O)-, and $-S(O)_2-$; and

each R^y is selected from the group consisting of hydrogen and hydroxy; and

each R^{x2} is selected from the group consisting of hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, alkoxyalkoxy, R^b-oxyalkyl, alkenyloxy, alkynyloxy, R^bR^b-amino, R^bR^b-aminoalkyl, R^bR^b-aminoalkoxy, R^bR^b-aminoalkyl(R^b)amino, carbocyclyl, carbocyclylalkyl, carbocyclyloxy, carbocyclyloxyalkoxy, heterocyclyl, heterocyclylalkyl, heterocyclyloxy, and heterocyclyloxyalkoxy, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

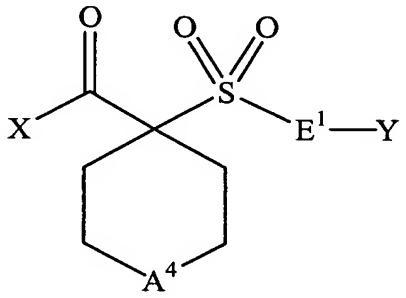
any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen and hydroxy; and

each R^b is independently selected from the group consisting of hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, bisalkoxyalkyl, alkylthioalkyl, alkylthioalkenyl, alkylsulfoxidoalkyl, alkylsulfonyl, alkylsulfonylalkyl, carbocyclyl, carbocyclylalkyl, carbocyclyloxyalkyl, carbocyclylalkoxyalkyl, carbocyclylthioalkyl,

carbocyclylthioalkenyl, carbocyclylsulfoxidoalkyl, carbocyclylsulfonyl, carbocyclylsulfonylalkyl, heterocyclyl, heterocyclylalkyl, heterocyclyloxyalkyl, heterocyclylalkoxyalkyl, heterocyclylthioalkyl, heterocyclylsulfoxidoalkyl, heterocyclylsulfonyl, heterocyclylsulfonylalkyl, aminoalkyl, aminosulfonyl, aminoalkylsulfonyl, and alkoxyalkylaminoalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkylcarbonyl, carbocyclyl, and carbocyclylalkyl.

78. A compound or salt thereof according to claim 77, wherein:
the compound corresponds in structure to Formula (78-1):



(78-1); and

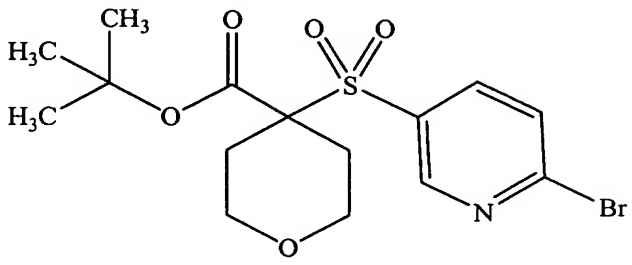
A^4 is selected from the group consisting of $-C(H)_2-$, $-C(R^x)(H)-$, $-C(R^x)_2-$, -O-, $-N(H)-$, $-N(R^x)-$, -S-, -S(O)-, and $-S(O)_2-$.

79. A compound or salt thereof according to claim 78, wherein Y is bromo.

80. A compound or salt thereof according to claim 78, wherein X is $-NH-O-R^2$, and R^2 is 2-tetrahydropyranyl.

81. A compound or salt thereof according to claim 78, wherein X is $-O-R^1$, and R^1 is selected from the group consisting of hydrogen and t-butyl.

82. A compound or salt thereof according to claim 81, wherein the compound corresponds in structure to Formula (82-1):



(82-1).

83. A compound or salt thereof according to claim 78, wherein E^1 is selected from the group consisting of furanyl, thienyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, thiodiazolyl, oxadiazolyl, pyrrolyl, pyrazolyl, imidazolyl, triazolyl, tetrazolyl, oxathiazolyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, triazinyl, oxathiazinyl, oxepinyl, thiepinyl, benzofuranyl, isobenzofuranyl, benzoxazolyl, benzoisoxazolyl, anthranilyl, benzothienyl, isobenzothienyl, benzothiazolyl, benzoisothiazolyl, benzothiadiazolyl, indolizinyl, pyranopyrrolyl, benzoxadiazolyl, indolyl, isoindazolyl, benzoimidazolyl, benzotriazolyl, purinyl, imidazopyrazinyl, imidazolopyridazyl, quinolinyl, isoquinolinyl, pyridopyridinyl, phthalazinyl, quinoxalinyl, benzodiazinyl, pteridinyl, pyridazinotetrazinyl, pyrazinotetrazinyl, pyrimidinotetrazinyl, benzoimidazothiazolyl, carbazolyl, and acridinyl, wherein:

any member of such group is substituted with one or more independently selected R^x substituents.